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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/631,874	07/31/2003	Indranil Nandi	G-33302P1	1795

72554 7590 10/30/2008

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
10/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/631,874	NANDI ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 04/16/08.

The amendment filed 04/16/08 affects the application, 10/631,874 as follows:

Claim 1 has been amended. New claim 21 has been added. The rejections of the prior office action are maintained.

The responsive to applicants' amendments is contained herein below.

Claims 1-21 are pending in the application

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In claim 1, applicant claims "A pharmaceutical composition comprising a tablet core consisting essentially of fexofenadine or a pharmaceutical acceptable acid addition salt thereof, about 10 wt. % to about 70 wt. % of lactose, and about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose, all of which are dispersed in the tablet core, wherein the weight percents are based on the total weight of the pharmaceutical composition." However, the recitation of the language "all of which are dispersed in the tablet core" in the claim constitutes new matter as set forth in the claim. More specifically, the specification does not

describe, disclose, provide or use any language or matter that pertains to any composition wherein all the said ingredients "are dispersed in the tablet core" as recited in the claim. Furthermore, the introduction of the said language "all of which are dispersed in the tablet core" as set forth in claim 1, constitutes new matter. On the contrary, it should be noted that the specification describes composition wherein said ingredient are mixed into a tablet. Moreover, the specification does not have support for the said language and consequently the claims contain new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Domet et al. (US 4,929,605) in combination with Maekawa et al. (US 4,176,175).

In claim 1, applicant claims "A pharmaceutical composition comprising a tablet core consisting essentially of fexofenadine or a pharmaceutical acceptable acid addition salt thereof, about 10 wt. % to about 70 wt. % of lactose, and about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose, all of which are dispersed in the tablet core, wherein the weight percents are based on the total weight of the pharmaceutical composition." Dependent claims 2-13 are drawn to specific wt. % and mg of the components of said composition. Claims 14-17 are drawn to low-substituted hydroxypropyl cellulose of specific average particle sizes and wt. %. Claim 21 is drawn to a tablet core comprising fexofenadine or a pharmaceutical

acceptable acid addition salt thereof, about 10 wt. % to about 70 wt. % of lactose, and about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose dispersed within a tablet core, wherein the weight percents are based on the total weight of the pharmaceutical composition.

Domet et al. disclose a pharmaceutical composition in solid unit dosage form containing a therapeutically effective amount of a piperidinoalkanol compound, such as fexofenadine and terfenadine, or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable nonionic or cationic surfactant, and a pharmaceutically acceptable carbonate salt. Furthermore, Domet et al. disclose that said piperidinoalkanol derivatives (compounds) which are antihistamines, antiallergic agents and bronchodilators, are in general, only minimally soluble in water and therefore the therapeutically inactive ingredients in a pharmaceutical composition containing one or more of these compounds are very important in providing for their efficient and immediate absorption and bioavailability after oral administration (see col. 1, lines 11-33). It should be noted that piperidinoalkanol compounds fexofenadine and terfenadine, which are useful as antihistamines, antiallergic agents and bronchodilators are quite similar in structure, differing only by a substituent (i.e. methyl group as opposed to a carboxyl group).

The difference between applicant's claimed composition and the composition disclosed by Domet et al. is that applicant's composition contains lactose and low-substituted hydroxypropyl cellulose.

Maekawa et al. disclose that solid drugs preparation (dosage form) such as tablets, granules and pill that are coated with sugars containing low-substituted hydroxypropyl cellulose improves the disintegration time (see abstract). Furthermore, Maekawa et al. disclose that sugars

in general such as sucrose (which like lactose is a disaccharide) can be used (see col. 2, lines 23-37).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Domet et al. and Maekawa et al., to have prepared a pharmaceutical composition comprising fexofenadine, low-substituted hydroxypropyl cellulose and lactose and to be used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine and terfenadine (after oral administration) and Maekawa et al. disclose that specific components such low-substituted hydroxypropyl cellulose and sugars such as lactose and improves the rapid disintegration and favorable release (i.e.,bioavailability) of drugs.

One having ordinary skill in the art would have been motivated in view of Domet et al. and Maekawa et al., to have prepared a pharmaceutical composition comprising fexofenadine, lactose and low-substituted hydroxypropyl cellulose to be used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine and terfenadine (after oral administration) and Maekawa et al. disclose that specific components such low-substituted hydroxypropyl cellulose and sugars such as lactose and improves the rapid disintegration and favorable release (i.e.,bioavailability) of drugs. It should be noted that the use of specific quantities (e.g., mg), wt. % and type of low-substituted hydroxypropyl cellulose of said composition depends on the need, such as the individual to which this composition is administered. It should also be noted that the use of lactose and low-substituted hydroxypropyl

cellulose in or within tablets (such as tablets core) along with active ingredients such as fexofenadine is common in the art and is well with the purview of a skilled artisan.

Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Domet et al. (US 4,929,605) in combination with Obara et al. (US 6,380,381 B1).

In claim 18, applicant claims "A method of preparing a pharmaceutical composition consisting essentially of fexofenadine or a pharmaceutical acceptable acid addition salt thereof, about 10 wt. % to about 70 wt. % of lactose, and about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose, wherein the weight percents are based on the total weight of the pharmaceutical composition, said method comprising:

(a) mixing fexofenadine, lactose, and low-substituted hydroxypropyl cellulose to form a premix;

(b) adding a solvent to the premix formed in Step (a) to form a wet granulation; and

(c) drying the wet granulation to form dried granules;

(d) mixing at least one excipient with the dried granules to form a pharmaceutical composition." Claim 19 is drawn to a method of preparing a pharmaceutical composition consisting essentially of fexofenadine or a pharmaceutical acceptable acid addition salt thereof, about 10 wt. % to about 70 wt. % of lactose, and about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose, wherein the weight percents are based on the total weight of the pharmaceutical composition, said method comprising: (a) mixing fexofenadine, lactose, and low-substituted hydroxypropyl cellulose to form a premix;…….. Claim 20 is drawn to

the method according to claim 19 further comprising the step of milling the dried using a conical screen.

Domet et al. disclose a method of preparing a pharmaceutical composition in solid unit dosage form containing a therapeutically effective amount of a piperidinoalkanol compound, such as fexofenadine and terfenadine comprising mixing said piperidinoalkanol compound with a pharmaceutically acceptable nonionic or cationic surfactant and a pharmaceutically acceptable carbonate salt and forming granules which are dried and milled to uniform size (see col. 4, lines 50-64). Furthermore, Domet et al. disclose that said piperidinoalkanol derivatives (compounds) which are antihistamines, antiallergic agents and bronchodilators, are in general, only minimally soluble in water and therefore the therapeutically inactive ingredients in a pharmaceutical composition containing one or more of these compounds are very important in providing for their efficient and immediate absorption and bioavailability after oral administration (see col. 1, lines 11-33). It should be noted that the piperidinoalkanol compounds fexofenadine and terfenadine, are useful as antihistamines, antiallergic agents and bronchodilators.

The difference between applicant's method and the method disclosed by Domet et al. is that applicant's uses low-substituted hydroxypropyl cellulose in their composition.

Obara et al. disclose that low-substituted hydroxypropyl cellulose exhibits good granulation characteristics and tablet properties (i.e. improving bioavailability) (see abstract). Furthermore, Obara et al. exemplify the preparation of a good granulation composition comprising the low-substituted hydroxypropyl cellulose and lactose (see col. 4, line 45-56). Also, Obara et al. disclose that for the low-substituted hydroxypropyl cellulose of the present invention, that tablet may be prepared that contain, for example, active ingredients, lubricants

(e.g., magnesium stearate), excipients (e.g., corn starch and lactose), and other disintegrators and binders (see col. 3, line 64 to col. 4, line 4). Obara et al disclose a low-substituted hydroxypropyl cellulose having a hydroxypropoxyl content in the range of 5.0 to 16.0% by weight and an apparent average degree of polymerization in the range of 350 to 700 (see abstract). In addition, Obara et al. disclose that low-substituted hydroxypropyl cellulose, its degree of substitution provides good granulation such that it improves the disintegration properties of tablets (i.e. improving bioavailability) (see col. 1, lines 21-59).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Domet et al. and Obara et al., to have used the method of Domet et al. to prepare a pharmaceutical composition comprising fexofenadine, low-substituted hydroxypropyl cellulose and lactose to be used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine (after oral administration) and Obara et al. disclose that a good granulation such as low-substituted hydroxypropyl cellulose and lactose improves the bioavailability (i.e. rapid disintegration and favorable release) of drugs.

One having ordinary skill in the art would have been motivated in view of Domet et al. and Obara et al., to have used the method of Domet et al. to prepare a pharmaceutical composition comprising fexofenadine, low-substituted hydroxypropyl cellulose and lactose to be used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine (after oral administration) and Obara et al. disclose that a good granulation such as low-substituted hydroxypropyl cellulose and lactose improves the bioavailability (i.e. rapid

disintegration and favorable release) of drugs. It should be noted that the use of specific quantities (e.g., mg), wt. % and type of low-substituted hydroxypropyl cellulose of said composition depends on the need, such as the individual to which this composition is administered. In addition, the use of specific mills such as a low shear mill is commonly used in the art in the preparation of such oral tablet formulations, and is well with the purview of a skill artisan does not appear to alter the said composition formed.

Response to Arguments

Applicant's arguments with respect to claim 1-21 have been considered but are not found convincing.

The applicant argues that Domet makes no mention of fexofenadine and states that terfenadine is the preferred active ingredient. However, Domet et al. disclose a piperidinoalkanol compound (e.g. compounds of the formula (3) (see col. 2, lines 36-63), which includes fexofenadine and terfenadine, are antihistamines, antiallergic agents and bronchodilators (i.e., they are functionally equivalent) (see also Domet et al., col. 42-44). Thus, it is obvious to one of ordinary skill in the art, based on Domet et al.'s teaching, to the substitute the functionally equivalent fexofenadine for terfenadine.

The applicant argues that the Maekawa patent, however, says absolutely nothing about lactose. While Maekawa repeatedly speaks of using "sugar", the only sugar specifically referred to in Maekawa is sucrose, not lactose. Consequently, then, one of skill following the teaching of Mackawa would have been lead to use sucrose rather than lactose in any pharmaceutical composition since this was clearly Maekawa's preferred (and apparently only) embodiment. On the contrary however, Maekawa et al. disclose that sugars in general such as sucrose (which like

lactose is a disaccharide) can be used (see col. 2, lines 23-37). Consequently, one of ordinary skill in the art following the teaching of Mackawa would have been motivated to any sugar taught by Mackawa, especially a disaccharide sugar such as lactose that is similar and common like sucrose base on factors such as availability, cost and/or need. Also, it should be noted that lactose and low-substituted hydroxypropyl cellulose are some of most commonly known compounds or substances that are used in tablets. Furthermore, it should also be noted that the use of lactose and low-substituted hydroxypropyl cellulose in or within tablets (such as tablets core) along with active ingredients such as fexofenadine is common in the art and is well with the purview of a skilled artisan.

The applicant argues that the Applicants have herein amended the claims to clarify that the fexofenadine (or a pharmaceutical acceptable acid addition salt thereof), lactose, low-substituted hydroxypropyl cellulose are dispersed in a tablet core. This provides yet another distinction between the subject matter of the claims and the teachings of Demot and Maekawa. The sugars and low-substituted HPC disclosed in Maekawa are applied as an outer coating.

The applicant argues that the Maekawa patent, however, says absolutely nothing about lactose. While Maekawa repeatedly speaks of using "sugar", the only sugar specifically referred to in Maekawa is sucrose, not lactose. Consequently, then, one of skill following the teaching of Mackawa would have been lead to use sucrose rather than lactose in any pharmaceutical composition since this was clearly Maekawa's preferred (and apparently only) embodiment. On the contrary however, Maekawa et al. disclose that sugars in general such as sucrose (which like lactose is a disaccharide) can be used (see col. 2, lines 23-37). Consequently, one of ordinary skill in the art following the teaching of Mackawa would have been motivated to any sugar

taught by Mackawa, especially a disaccharide sugar such as lactose that is similar and common like sucrose base on factors such as availability, cost and/or need. Also, it should be noted that lactose and low-substituted hydroxypropyl cellulose are some of most commonly known compounds or substances that are used in tablets. Furthermore, it should also be noted that the use of lactose and low-substituted hydroxypropyl cellulose in or within tablets (such as tablets core) along with active ingredients such as fexofenadine is common in the art and is well with the purview of a skilled artisan.

The applicant argues that as for the Obara patent, this reference merely discloses "low-substituted hydroxypropyl cellulose having good granulation characteristics and tablet properties." See Obara, Col. 1, lines 6 - 8. Obara says nothing about using this low-substituted hydroxypropyl cellulose with fexofenadine or any other form of piperidinoalkanol derivative. In fact, Obara does not specify any form of active pharmaceutical ingredient which is said to be suitable for use with the low- substituted hydroxypropyl cellulose described therein. However, Domet et al. disclose that said piperidinoalkanol derivatives (compounds) which are antihistamines, antiallergic agents and bronchodilators, are in general, only minimally soluble in water and therefore the therapeutically inactive ingredients in a pharmaceutical composition containing one or more of these compounds are very important in providing for their efficient and immediate absorption and bioavailability after oral administration (see col. 1, lines 11-33). It should be noted that the piperidinoalkanol compounds fexofenadine and terfenadine, are useful as antihistamines, antiallergic agents and bronchodilators. Consequently, One having ordinary skill in the art would have been motivated in view of Domet et al. and Obara et al., to have used the method of Domet et al. to prepare a pharmaceutical composition comprising fexofenadine,

low-substituted hydroxypropyl cellulose and lactose to be used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine (after oral administration) and Obara et al. disclose that a good granulation such as low-substituted hydroxypropyl cellulose and lactose improves the bioavailability (i.e. rapid disintegration and favorable release) of drugs (also see above rejection).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
October 25, 2008.

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623